


Relation of the C/T-13910 LCT Polymorphism with Body Composition Measures and Their Modulation by Dairy Products in a Caucasian Men

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Abstract

The C/T-13910 LCT is closely associated with lactase persistence and LCT has emerged as a new candidate gene for obesity, in particular in northern Europeans. The aim of this research is to investigate to what degree sex determines the association between the LCT variant and anthropometric traits in a cohort of healthy individuals. We recruited 1000 (500 males and 500 females aged 18–65 years) healthy blood donors. The C/T-13910 LCT polymorphism was genotyped using TaqMan assays. All individuals were phenotyped with respect to anthropometric characteristics. Prevalence of genotypes was 22.7% CC (lactase non-persistent, LNP), 58.6% CT, and 18.7% TT. LNP genotype was present less frequently among men $p = .0005$; OR 0.582 [0.425–0.794]. Therefore, in addition statistical calculations were performed separately for men and women. Additional analysis demonstrated an association between the CC genotypes and higher chest ($p = .03$), waist ($p = .005$), and forearm circumference ($p = .0004$) or more lean body mass ($p = .04$), than T-allele carriers in males. In females, they were not significantly different. Men consumed more milk ($p = .003$), while women ate more yoghurt ($p = .001$). Pearson's correlation analysis showed that the higher intake of milk and dairy products was associated with higher fat body mass among men with lactase persistence. In Caucasian men, the LNP genotype is associated with reduced milk intake and dairy products, but more fat-free mass and higher forearm circumference, which may be relevant to dietary management for lactose intolerant.

Keywords

anthropometric measures, fat-free mass, lactase non-persistent, milk intake, dairy products, nutrigenetics

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Introduction

Lactase (LCT) is an inner membrane lipoprotein belonging to the β -galactosidases, with biological role being the distribution of lactose to galactose and glucose which, as monosaccharides, can be absorbed into the blood. LCT is absent in dividing crypt enterocytes. It is located at the tip of intestinal villi and is present in the absorption enterocyte membrane as a precursor of molecular weight 220 Da which, during transport via cytoplasm, goes through a process of post-translational modification and reaches the cell membrane as a protein of weight 150 kDa. Lactase expression is the highest in the central part of the jejunum, with a decreasing tendency in the proximal (duodenum) and distal (ileum) directions. The fact that lactase is located at the tips of intestinal villi can lead to disease

processes, which induce mucous membrane damage, contributing to a decrease in the number of lactase molecules and lowering the activity of this enzyme in the bowel (Heyman, 2006; Lomer et al., 2008; Madry et al., 2010; Mattar et al., 2012).

Congenital lactase deficiency is a genetically conditioned disease characterized by total lactase deficiency. This metabolic defect appears very rarely (1 in 60 cases)

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(Kuokkanen et al., 2006). The most common type of primary enzymatic deficiency is adult-type lactase deficiency. Two phenotypes have been distinguished: maintained high activity of lactase during one's lifetime and decreasing lactase activity (which was correct in early childhood) with age—that is, adult-type hypolactasia—and secondary lactase deficiency appearing during digestive system diseases as a result of damage to the brush border or reduction of intestinal area, usually lasting for a few weeks (Aurisicchio & Pitchumoni, 1994; Mattar et al., 2012; Troelsen, 2005).

Maintaining a high activity of lactase after infancy and keeping it at the same level in adulthood is an adaptive characteristic. Lactose tolerance is considered to be an autosomal-dominant genetic feature, although the actual levels of lactase in intestinal mucosa show a trimodal distribution, with very low levels in homozygous people for the lactase non-persistence variant (LNP) (Kuokkanen et al., 2003). Lactase persistence (LP), which is the ability to digest lactose throughout adulthood, occurs in most residents of northern Europe (in 73%–95% in the British Isles and Scandinavia), but is less common in eastern and southern Europe (6%–36%) (Itan et al., 2009). LP dominates over LNP (Sahi, 1994).

The LCT gene is 49.3 kb in length and located on the long (q) arm of chromosome 2 at position 21 (containing 17 exons and translated into a 6 kb transcript) (Boll et al., 1991). A single nucleotide polymorphic variant (SNP), C/T-13910 LCT (rs4988235; Chr.2: 135851076 on GRCh38), in intron 13 of the MCM6 gene which is 13.910 bp from the initiation codon of LCT has been identified, in recent years, as the major genetic determinant of lactose maldigestion (Rasinpera et al., 2004, 2005). The functional role of MCM6 in vertebrates is unknown but has been implicated in “licensing” DNA replication during the cell cycle. This association has been confirmed in a study of DNA collected from individuals of Finnish, South Korean, Italian, German, French, or white or African North American descent (Enattah et al., 2002; Rasinpera et al., 2004; Troelsen, 2005).

Indeed, a genome-wide association study (GWAS) published in 2009 carried out by Cohorts for Heart and Aging Research in Genome Epidemiology (CHARGE) (Heard-Costa et al., 2009) found an association with central abdominal fat in the LCT region, confirmed in individuals of Caucasian origin (Corella et al., 2011). This association led by C/T-13910 polymorphism, was further replicated in a meta-analysis of eight European cohorts, corroborating its role in some anthropometric measurements and obesity regulation (Kettunen et al., 2010).

To date, the research has been based on small research groups (Khabarova et al., 2009; Madry et al., 2010), mainly among children and teenagers (Almon et al.,

2011; Madry et al., 2010), elderly people (Corella et al., 2011; Smith et al., 2009), or the sick (Travis et al., 2013). There is a lack of population-based research concerning healthy middle-aged people of both sexes, using exact anthropometric measurements estimating the amount of adipose tissue and non-fat mass. Only in this way is there a possibility to evaluate not only the risk of obesity but also correlation between body build, body composition in relations to and C/T-13910 polymorphism.

The analysis of the frequency of LCT polymorphisms, along with measurements of body proportions in a cohort of healthy individuals, was performed in order to verify the hypothesis of association between the examined SNP and anthropometric variables. The main aim was to identify a measurement which is connected to the C/T-13910 LCT polymorphism with respect to gender differences.

Several studies have linked the CC genotype with a lower consumption of dairy products (Laaksonen et al., 2009; Lehtimäki et al., 2006; Tornaiainen et al., 2007), but this association has not always at a significant level (Gugatschka et al., 2005, 2007; Smith et al., 2009). Therefore, our secondary objective was to analyze the correlation of the C/T-13910 LCT polymorphism with obesity and obesity-related variables, as well as its relationship with lactose intake in a Polish population. We analyzed whether the C/T-13910 LCT polymorphism predicted complete milk abstinence.

Materials and Methods

Study Population and Data Source

A cohort of 1000 (median age 24 years; mean 27 years; range 18–65 years) blood donors from the Regional Blood Donor Center in Szczecin (Poland) was investigated, including 500 females (median age 22.5 years; mean 27.1 ± 10.2 years; range 18–65 years) and 500 males (median age 26 years; mean 27.8 ± 8.3 years; range 18–62 years). All subjects had medical examination data, as a good state of health is a prerequisite to qualify for blood donation. Consent was obtained from each person who was included in the study. The research was conducted from October to December 2011. The study was approved by the Bioethical Committee of the Pomeranian Medical University in Szczecin, no. KB-0012/57/11 and conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Main inclusion criteria for the study were: good health fulfilling World Health Organization criteria, including: age 18–65 years; weight at least 50 kg; a hemoglobin level of not less than 12.0 g/dl for females and not less than 13.0 g/dl for males as the threshold.

Main exclusion criteria for the study were: periodic disease outbreaks; a tattoo or body piercing, surgical

procedures, endoscopic and other diagnostic tests, treated with blood and blood products for 6 months from the date of the procedure; travel-associated risk of infections e.g. malaria or West Nile virus; emerging infectious diseases, for example, the Zika virus epidemics; health condition, including reduced hemoglobin levels.

Genotyping

DNA from peripheral blood mononuclear cells was isolated using the DNeasy Blood & Tissue Kit (Qiagen). Oligonucleotide primers and TaqMan probes for C/T-13910 LCT polymorphism (rs 4988235) were designed and synthesized by Applied Biosystems (ID: C_15769614_10). The fluorescence data were analyzed with the allelic discrimination 7500 Software, v.2.0.2. (Applied Biosystems, USA).

Anthropological Examination

Anthropometric measurements taken with a medical scale, an anthropometer, and an anthropological centimeter (body mass, height, hip, chest, shin, and forearm measurements) served as the basis for calculating the body mass index (BMI). The following formula was applied: $BMI = \text{weight [kg]} / (\text{height [m]})^2$. The range of the BMI values according to the World Health Organization (WHO, 1995) was taken into consideration. Adipose tissue distribution was assessed using the waist-to-hip ratio (WHR). Then, in accordance with the anatomical classification of obesity, two types of obesity were singled out: android and gynoid.

Lean muscle mass (including muscle, organs, and bone) was determined using Piechaczek's formula [27] for men: $-103.85484 + (0.446921 \times \text{body height [cm]}) + (0.13343 \times \text{hip circumference [cm]}) + (0.458056 \times \text{chest circumference [cm]}) + (0.838393 \times \text{shin circumference [cm]})$; and for women: $-61.719697 + (0.339491 \times \text{body height [cm]}) + (0.540846 \times \text{shin circumference [cm]}) + (0.26024 \times \text{chest circumference [cm]}) + (0.407343 \times \text{forearm circumference [cm]})$.

Body fat mass (in kilograms) was calculated using the formula $\text{body mass [kg]} - \text{lean muscle mass [kg]}$. Lean muscle mass (in percentage) was calculated as $(\text{lean muscle mass [kg]} / \text{body mass [kg]}) \times 100\%$. Total fat in percentage was calculated as $100\% - \text{lean muscle mass \%}$.

Survey Research

For survey research, a self-designed questionnaire was used. It consisted of metrics with socio-demographic data (e.g., sex, education, age, place of birth, place of residence) and questions concerning the amounts and frequency of intake of chosen dairy products (e.g., farm cheese, yoghurt, buttermilk).

Statistical Analysis

Each participant was identified by a code used in a database. The description of categorical variables (sex, genotype, and allele) was performed by frequency analysis (Fisher's exact test). Odds ratio (OR) 95% confidence interval (CI) and *p*-value for each variable were also estimated. In addition, Hardy Weinberg equilibrium was tested. We applied *t*-tests to normally distributed variables but, in order to analyze dairy product consumption (which did not follow a normal distribution), we applied the non-parametric Mann–Whitney U-test.

For further analysis—univariable logistic regression models for quantitative variables were calculated among males, where dependent variable was lactase persistent status. Due to existence of significant correlations between anthropometric parameters—multivariable analysis were not performed.

All statistical analyses were performed using R statistical environment—R version 4.0.3 (2020-10-10). Data are shown as mean and standard deviation. A *p* value of $<.05$ was considered to be statistically significant.

In order to determine the influence of variables concerning the amount of milk-products consumption on anthropometric parameters—Pearson's correlation coefficients and linear regression models were calculated. Pearson's correlation coefficient measured the strength and direction of association between two ranked variables. Size of Correlation Interpretation: .90 to 1.00 (−.90 to −1.00) - to .70 (−.50 to −.70) - moderate positive (negative) correlation; .30 to .50 (−.30 to −.50) - low positive (negative) correlation; .00 to .30 (.00 to −.30) - negligible correlation. *p*-values of less than .05 were considered to be statistically significant.

Results

Table 1 lists the general characteristics of the study subjects by gender. Adult women and men in the selected group were of comparable age.

Prevalence of genotype was: 22.7% CC (LNP), 58.6% CT, and 18.7% TT. The genotype and allele frequency distributions recorded for the analyzed SNP are presented in Table 2. A significant difference in genotype frequency in the C/T-13910 LCT polymorphism between males and females was found (Table 2). The CC genotype was present less frequently (18.0% vs. 27.4% in females; $p = .0005$; OR 1.719 [1.272–2.323]), where the CT genotype was represented more frequently (64.6% vs. 52.6% in females; $\chi^2 = 14.8$; $p < .0001$; OR 0.574 [0.444–0.741]).

Taking into account that the genetically defined LP follows a dominant model, CT and TT subjects (LP) were grouped and compared with CC subjects for the statistical analysis, as this dominant model has been observed in the European population. CT and TT individuals did not

Table 1. Anthropometric Characteristics of the Study Group.

Anthropometric variables	Male		Female	
	Range Min–Max	(n= 500) mean \pm SD	Range Min–Max	(n = 500) Mean \pm SD
Age (years)	18–62	27.8 \pm 8.3	18–65	27.1 \pm 10.2
Height (m)	157–200	180.0 \pm 8.3	147–190	166.4 \pm 6.0
Weight (kg)	50–150	83.5 \pm 14.3	45–110	65.1 \pm 11.1
Body mass index (kg/m ²)	17.5–45.3	25.7 \pm 4.0	16.3–40.9	23.5 \pm 3.9
Waist circumference (cm)	64–145	90.1 \pm 11.6	57–120	79.4 \pm 11.8
Hip circumference (cm)	77–155	103.9 \pm 8.1	78–138	100.2 \pm 8.4
Chest circumference (cm)	70–144	92.4 \pm 9.5	60–114	79.3 \pm 8.9
Forearm circumference (cm)	16–45	27.7 \pm 3.2	19–37	23.6 \pm 2.4
Shin circumference (cm)	26–56	37.7 \pm 3.8	22–50	35.9 \pm 3.4
Fat mass (%)	11.9–48.0	33.2 \pm 5.4	11.1–50.7	31.0 \pm 5.7
Fat mass (kg)	8.1–64.2	28.4 \pm 9.2	5.1–52.2	20.6 \pm 7.2
Lean mass (%)	52.0–88.1	66.8 \pm 5.4	49.3–88.9	69.0 \pm 5.7
Lean mass (kg)	39.9–85.8	55.1 \pm 6.1	31.2–62.6	44.5 \pm 5.0

Table 2. Distribution of LCT-13910C>T Polymorphism and Allele Frequencies Among Female and Male Subjects.

Allele/ genotype	Female (%) (n = 500)	Male (%) (n = 500)	p	OR (95% CI)
C/T	537/463 (53.7/46.3)	503/497 (50.3/49.7)	.13	1.187 (0.863–1.632)
CC	137 (27.4)	90 (18.0)	.0005*	1.719 (1.272–2.323)
CT	263 (52.6)	323 (64.6)	.0001*	
TT	100 (20.0)	87 (17.4)	0.33	0.574 (0.444–0.741)

Note. *Bold font indicates statistical significance.

Table 3. Association of the LCT-13910C>T Polymorphism with Anthropometric Variables in Caucasian Population (mean \pm SD).

Anthropometric variables	CC	CT/TT	p
	(n= 227)	(n = 773)	
Age (years)	27.8 \pm 9.6	27.3 \pm 9.3	.50
Height (m)	172.4 \pm 9.2	173.4 \pm 9.5	.14
Weight (kg)	73.7 \pm 16.5	74.5 \pm 15.5	.49
Body mass index (kg/m ²)	24.7 \pm 4.4	24.6 \pm 3.9	.92
Waist circumference (cm)	84.8 \pm 13.5	84.8 \pm 12.7	.99
Hip circumference (cm)	101.9 \pm 8.9	102.1 \pm 8.4	.77
Chest circumference (cm)	85.1 \pm 12.2	86.1 \pm 11.0	.26
Forearm circumference (cm)	25.5 \pm 4.02	25.7 \pm 3.3	.56
Shin circumference (cm)	36.6 \pm 4.1	36.9 \pm 3.6	.28
Fat mass (%)	32.3 \pm 5.9	32.1 \pm 5.6	.63
Fat mass (kg)	24.5 \pm 9.6	24.5 \pm 8.9	.96
Lean mass (%)	67.744 \pm 5.883	67.9 \pm 5.6	.63
Lean mass (kg)	49.2 \pm 8.0	49.9 \pm 7.6	.18

differ from the CC individuals in the whole population (Table 3); however, these association was different when females and males were examined separately.

The most important association was obtained with anthropometric measurements. Analysis of anthropometric parameters suggested significant dependence between CC

Table 4a. Association of the LCT-13910C>T Polymorphism with Anthropometric Variables Among Males (mean \pm SD).

Anthropometric variables	CC	CT/TT	p
	(n = 90)	(n = 410)	
Age (years)	28.3 \pm 8.2	27.7 \pm 8.4	.54
Height (m)	180.5 \pm 7.3	179.9 \pm 6.9	.47
Weight (kg)	85.9 \pm 16.0	83.0 \pm 13.9	.08
Body mass index (kg/m ²)	26.3 \pm 4.4	25.6 \pm 3.9	.13
Waist circumference (cm)	93.3 \pm 11.9	89.4 \pm 11.5	.004*
Hip circumference (cm)	104.8 \pm 9.2	103.7 \pm 7.9	.27
Chest circumference (cm)	94.4 \pm 10.3	91.9 \pm 9.3	.03*
Forearm circumference (cm)	28.8 \pm 3.6	27.5 \pm 3.0	.0004*
Shin circumference (cm)	37.8 \pm 4.1	37.6 \pm 3.7	.67
Fat mass (%)	33.4 \pm 6.4	33.2 \pm 5.2	.71
Fat mass (kg)	29.5 \pm 10.6	28.1 \pm 8.8	.18
Lean mass (%)	66.6 \pm 6.4	66.8 \pm 5.2	.71
Lean mass (kg)	56.3 \pm 6.5	54.9 \pm 5.9	.04*

Note. *Bold font indicates statistical significance.

genotype and CT+TT genotypes for higher chest circumference (94.4 \pm 10.3 vs. 91.9 \pm 9.3 cm, $p = .03$), higher waist circumference (93.3 \pm 11.9 vs. 89.4 \pm 11.5 cm, $p = .004$), higher forearm circumference (28.8 \pm 3.6 vs. 27.5 \pm 3.0 cm, $p = .0004$), and higher lean muscle mass percentage (56.3 \pm 6.5 vs. 54.9 \pm 5.9 kg, $p = .04$) among males (Table 4a). We observed that the C/T-13910 LCT SNP presented a strong association with anthropometric measures in males (Table 4b), while in females (Table 4c) these were not significantly different.

Overall, 37.4% of studied individuals were overweight (i.e., with BMI > 25 kg/m²) and an increased prevalence of overweight individuals (i.e., BMI 25 > kg/m²) was detected among T-allele carriers, as compared to individuals with the CC genotypes. (females: 69.6% vs. 30.4%; males: 80.3% vs. 19.6%). Anthropometric analyses showed that 17.6% of females and 2.6% males were at a higher risk of android obesity type, while others were at a risk of (or suffered from) gynoid obesity type. Analysis of 51.2% of males with BMI < 25 showed statistically different results within waist circumference (86.1 \pm 8.6 vs. 82.1 \pm 7.2 cm, $p = .002$) and forearm circumference (27.0 \pm 2.3 vs. 26.2 \pm 2.6 cm, $p = .04$); see Table 5a. T-allele carriers had lower measurements than LNP individuals. Among males with obesity (BMI > 25), only forearm circumference was statistically different (30.3 \pm 3.9 vs. 28.9 \pm 2.7 cm, $p = .006$); see Table 5b. CC individuals had higher measurements. Grouping according to BMI index did not show any statistically significant differences among women (Table 5c and 5d).

Tables 6–15 show the mean intakes of milk and dairy products (total and by gender), depending on the C/T-13910 LCT genotypes. The results are shown by grouping the T carriers together (LP) and comparing them with CC

subjects (LNP). Statistical analysis of milk intake (in glasses; 1 glass = 11.5 g of lactose) among the investigated people during a week showed a statistically significant difference; that is, men drank more milk (6.6 \pm 0.3) than women (5.0 \pm 0.2), $p = .001$; see Table 11. Correlation between daily and weekly milk intake and genotype showed significant differences among men (174.6 \pm 189.2 vs. 229.6 \pm 252.6 g/day, $p = .05$; and 1221.6 \pm 1324.5 vs. 1607.5 \pm 1767.9 g/week, $p = .001$, respectively); see Tables 9 and 12. Among women with LP genotype, the daily and weekly intake of milk was higher than among women with NLP genotype; however, values were statistically significant only while analyzing weekly intake of milk (1106.4 \pm 1253.7 vs. 1272.3 \pm 1271.2 g/week, $p = .02$, Table 13). Analyzing the results per gender, it can be observed that LP consumed more milk and dairy products. Men drank more milk (1607.5 \pm 1767.9 vs. 1272.3 \pm 1271.2 g/week in females, $p = .003$; and 229.6 \pm 252.6 vs. 181.8 \pm 181.6 g/day in females, $p = .003$), while women ate more yoghurt (743.4 \pm 731.4 vs. 613.5 \pm 721.4 g/week in males, $p = .01$; and 106.2 \pm 104.5 vs. 87.7 \pm 103.1 g/day in males, $p = .01$); see Tables 14 and 15.

The analysis of weekly milk and dairy product intake (e.g., farm cheese, yoghurt, buttermilk) per grams of lactose, in the context of genotype of investigated individuals, showed no statistically significant values during the analysis of CC vs. CT and TT genotypes, nor in the whole investigated population or in the analysis concerning sex.

Only 14.2% (142 individuals), of which 28.8% were CC subjects, reported digestive tract problems after the consumption of milk. Such problems were reported by 17.8% of women and 10.6% of men, where 5% of individuals had stomach aches, 4.7% reported diarrhea, 7.7% had intestinal gases, and 2.2% nausea and vomiting.

Table 4b. Association of the LCT-13910C>T Polymorphism with Anthropometric Variables Among Males (logistic regression models).

Anthropometric variables	OR	95% CI	<i>p</i>
Age (years)	1.01	0.98–1.04	.54
Height (m)	1.01	0.98–1.05	.47
Weight (kg)	1.01	1.00–1.03	.08
Body mass index (kg/m ²)	1.04	0.99–1.10	.13
Waist circumference (cm)	1.03	1.01–1.05	<.01*
Hip circumference (cm)	1.02	0.99–1.04	.27
Chest circumference (cm)	1.03	1.00–1.05	.03*
Forearm circumference (cm)	1.12	1.05–1.20	<.01*
Shin circumference (cm)	1.01	0.95–1.07	.67
Fat mass (%)	1.01	0.97–1.05	.70
Fat mass (kg)	1.02	0.99–1.04	.18
Lean mass (%)	0.99	0.95–1.03	.70
Lean mass (kg)	1.04	1.00–1.08	.04*
Milk (g/week)	1.00	1.00–1.00	.05
Milk (g/day)	1.00	1.00–1.00	.05
Lactose (g/week)	1.00	0.99–1.00	.05
Lactose (g/day)	0.98	0.95–1.00	.05
Yoghurt (g/week)	1.00	1.00–1.00	.24
Yoghurt (g/day)	1.00	1.00–1.00	.24
Curd (g/week)	1.00	1.00–1.00	.48
Curd (g/day)	1.00	1.00–1.01	.49
Total dairy products (g/week)	1.00	1.00–1.00	.29
Total dairy products (g/day)	1.00	1.00–1.00	.29

Note. *Bold font indicates statistical significance.

Table 4c. Association of the LCT-13910C>T Polymorphism with Anthropometric Variables Among Females (mean ± SD).

Anthropometric variables	CC	CT/TT	<i>p</i>
	(<i>n</i> = 137)	(<i>n</i> = 363)	
Age (years)	27.5 ± 10.4	27.0 ± 10.1	.60
Height (m)	167.04 ± 5.6	166.1 ± 6.2	.12
Weight (kg)	65.7 ± 11.1	64.9 ± 11.2	.49
BMI (kg/m ²)	23.6 ± 4.1	23.5 ± 3.8	.88
Waist circumference (cm)	79.2 ± 11.5	79.5 ± 11.9	.79
Hip circumference (cm)	100.1 ± 8.2	100.2 ± 8.6	.79
Chest circumference (cm)	79.1 ± 9.1	79.4 ± 8.9	.64
Forearm circumference (cm)	23.4 ± 2.6	23.7 ± 2.4	.31
Shin circumference (cm)	35.7 ± 3.7	36.0 ± 3.3	.46
Fat %	31.5 ± 5.4	30.7 ± 5.8	.20
Fat kg	21.1 ± 7.2	20.4 ± 7.2	.32
Active tissue %	68.5 ± 5.4	69.2 ± 5.8	.20
Active tissue kg	44.5 ± 4.8	44.5 ± 5.1	.92

Linear regression analysis showed (Table 16) that the higher intake of milk, dairy products, and lactose (per week) were associated with higher fat mass ($r = .30, p = .003$; $r = .30, p = .004$; and $r = .30, p = .004$, respectively) among males with LP genotype. There was no correlation was in females with LP genotype.

Discussion

The T-allele of the C/T-13910 LCT polymorphism has been subjected to a strong positive selection in recent history, enabling an unrestricted diet concerning milk and milk products (Bersaglieri et al., 2004) and is

Table 5a. Association of the LCT-13910C>T Polymorphism with Anthropometric Variables Among Males with BMI < 25 (mean \pm SD).

Anthropometric variables	CC	CT/TT	p
	(n = 41)	(n = 210)	
Age (years)	27.0 \pm 7.1	25.3 \pm 7.1	.14
Height (m)	180.6 \pm 7.5	180.4 \pm 6.5	.87
Weight (kg)	73.9 \pm 8.5	74.0 \pm 7.6	.97
Body mass index (kg/m ²)	22.6 \pm 2.0	22.7 \pm 1.6	.85
Waist circumference (cm)	86.1 \pm 8.6	82.1 \pm 7.2	.002*
Hip circumference (cm)	98.7 \pm 5.5	99.3 \pm 5.6	.56
Chest circumference (cm)	87.7 \pm 6.0	86.2 \pm 6.0	.14
Forearm circumference (cm)	27.0 \pm 2.3	26.2 \pm 2.6	.04*
Shin circumference (cm)	35.4 \pm 3.0	35.6 \pm 2.8	.62
Fat mass (%)	28.5 \pm 5.0	29.7 \pm 3.5	.07
Fat mass (kg)	21.3 \pm 5.3	22.1 \pm 4.2	.32
Lean mass (%)	71.5 \pm 5.0	70.3 \pm 3.5	.07
Lean mass (kg)	52.6 \pm 4.7	51.9 \pm 4.6	.38

Note. *Bold font indicates statistical significance.

Table 5b. Association of the LCT-13910C>T Polymorphism with Anthropometric Variables Among Males with BMI \geq 25 (mean \pm SD).

Anthropometric variables	CC	CT/TT	p
	(n = 49)	(n = 200)	
Age (years)	29.3 \pm 9.1	30.2 \pm 8.9	.53
Height (m)	180.4 \pm 7.3	179.4 \pm 7.4	.39
Weight (kg)	95.9 \pm 13.8	92.5 \pm 12.6	.09
Body mass index (kg/m ²)	28.4 \pm 3.5	28.7 \pm 3.2	.17
Waist circumference (cm)	99.3 \pm 11.0	97.1 \pm 10.0	.19
Hip circumference (cm)	109.8 \pm 8.6	108.4 \pm 7.2	.22
Chest circumference (cm)	100.0 \pm 9.8	98.1 \pm 8.2	.15
Forearm circumference (cm)	30.3 \pm 3.9	28.9 \pm 2.7	.006*
Shin circumference (cm)	39.9 \pm 3.8	39.8 \pm 3.4	.84
Fat mass (%)	37.5 \pm 4.3	36.9 \pm 3.9	.29
Fat mass (kg)	36.4 \pm 8.9	34.4 \pm 7.9	.13
Lean mass (%)	62.5 \pm 4.3	63.1 \pm 3.9	.29
Lean mass (kg)	59.5 \pm 6.3	58.0 \pm 5.6	.11

Note. *Bold font indicates statistical significance.

considered a prime example of human genetic adaptation (Enattah et al., 2008; Tishkoff et al., 2007). T-allele prevalence has been shown to vary across European populations (Itan et al., 2009). LP ranges in frequency from 15%–54% in Eastern and Southern Europe, to 62%–86% in Central and Western Europe (Bersaglieri et al., 2004). This corresponds with our research concerning Polish population (Central Europe), where the prevalence of genotypes was: 22.7% CC (lactase nonpersistent; LNP), 58.6% CT, and 18.7% TT. Similarly, prevalence of genotypes was: 38.0% CC, 45.7% CT, and 16.3% TT in Mediterranean population (Corella et al., 2011). This

makes the LCT-13910 T allele a good candidate for predicting LP in Europe.

We found a relevant association with anthropometric measurements among LP and LNP subjects. The gender differences observed in our results are interesting. Interestingly, in our study, the CC genotype occurred almost two times more frequently in females than in males. It was found that male LNP allele carriers exhibited significantly increased waist circumference, chest circumference, forearm circumference, and lean muscle mass, whereas none of these associations were significant in females. Larson et al. (Larson et al., 2006) also

Table 5c. Association of the LCT-13910C>T Polymorphism with Anthropometric Variables Among Females with BMI < 25 (mean \pm SD).

Anthropometric variables	CC	CT/TT	p
	(n = 99)	(n = 276)	
Age (years)	25.2 \pm 7.8	25.0 \pm 8.5	.87
Height (m)	167.4 \pm 5.1	166.2 \pm 6.2	.10
Weight (kg)	60.5 \pm 5.6	60.3 \pm 6.1	.80
BMI (kg/m ²)	21.6 \pm 1.8	21.8 \pm 1.84	.30
Waist circumference (cm)	74.2 \pm 8.3	75.5 \pm 8.6	.32
Hip circumference (cm)	96.6 \pm 5.1	97.1 \pm 5.7	.44
Chest circumference (cm)	75.0 \pm 5.3	76.1 \pm 5.6	.10
Forearm circumference (cm)	22.7 \pm 2.3	23.1 \pm 2.2	.11
Shin circumference (cm)	34.7 \pm 3.0	35.1 \pm 2.7	.26
Fat %	29.2 \pm 3.8	28.6 \pm 4.4	.26
Fat kg	17.8 \pm 3.4	17.4 \pm 3.8	.31
Active tissue %	70.8 \pm 3.8	71.4 \pm 4.4	.26
Active tissue kg	42.9 \pm 3.7	42.9 \pm 4.0	.88

Table 5d. Association of the LCT-13910C>T Polymorphism with Anthropometric Variables Among Females with BMI \geq 25 (mean \pm SD).

Anthropometric variables	CC	CT/TT	p
	(n = 38)	(n = 87)	
Age (years)	33.5 \pm 13.5	33.0 \pm 12.5	.86
Height (m)	166.0 \pm 6.8	165.5 \pm 6.1	.72
Weight (kg)	79.0 \pm 10.7	79.4 \pm 11.1	.87
BMI (kg/m ²)	28.7 \pm 3.8	28.9 \pm 3.4	.77
Waist circumference (cm)	91.4 \pm 9.7	92.3 \pm 11.8	.68
Hip circumference (cm)	109.0 \pm 8.0	110.3 \pm 8.4	.42
Chest circumference (cm)	89.6 \pm 8.4	90.2 \pm 8.8	.71
Forearm circumference (cm)	25.3 \pm 2.5	25.4 \pm 2.0	.81
Shin circumference (cm)	38.4 \pm 4.2	38.9 \pm 3.3	.50
Fat %	37.4 \pm 4.3	37.5 \pm 4.2	.93
Fat kg	20.4 \pm 7.2	21.1 \pm 7.2	.85
Active tissue %	62.6 \pm 4.3	62.5 \pm 4.2	.93
Active tissue kg	44.5 \pm 5.1	44.5 \pm 4.9	.62

Table 6. Association of the LCT-13910C>T Polymorphism with Average Consumption of Dairy Products in Caucasian Population (mean \pm SD).

Anthropometric variables	CC	CT/TT	p
	(n = 227)	(n = 773)	
Milk (g/day)	164.6 \pm 182.9	207.2 \pm 223.2	.008*
Yoghurt (/day)	94.9 \pm 94.2	96.4 \pm 104.1	.85
Curd (g/day)	30.9 \pm 44.9	30.6 \pm 44.6	.94
Total dairy products (g/day)	290.3 \pm 242.2	334.1 \pm 279.1	.03*
Lactose (g/day)	14.0 \pm 11.8	16.2 \pm 13.7	.03*

Note. *Bold font indicates statistical significance.

found differences in these issues, in the context of sex. According to their research, LP is associated with increased BMI, leg adiposity, trunk adiposity, and waist

circumference among boys. The authors investigated the young and explained their results with by fact that girls consumed less lactose than boys, such that the

Table 7. Association Between Anthropometric Variables and Total Dairy Products (g/day) and Lactose (g/day).

Anthropometric variables	Total dairy products (g/day)		Lactose (g/day)	
	Correlation	<i>p</i>	Correlation	<i>p</i>
Age (years)	0.02	.62	0.07	.82
Height (m)	0.08	.02	0.78	.01*
Weight (kg)	0.11	.0009	0.10	.001*
Body mass index (kg/m ²)	0.08	.009	0.08	.01*
Waist circumference (cm)	0.08	.01	0.08	.01*
Hip circumference (cm)	0.10	.002	0.10	.002*
Chest circumference (cm)	0.11	.0003	0.11	.0004*
Forearm circumference (cm)	0.05	.09	0.05	.09
Shin circumference (cm)	0.06	.07	0.06	.08
Fat mass (%)	0.07	.04	0.06	.05*
Fat mass (kg)	0.10	.002	0.10	.003*
Lean mass (%)	-0.07	.04	-0.06	.05*
Lean mass (kg)	0.10	.001	0.10	.001*

Note. *Bold font indicates statistical significance

Table 8. The Average Daily Consumption of Milk, Yoghurt, Curd, Total Dairy Products and Lactose in Caucasian Population (g/day) (mean ± SD).

	Male	Female	<i>p</i>
	(<i>n</i> = 500)	(<i>n</i> = 500)	
Milk (g/day)	219.7 ± 243.1	175.3 ± 181.0	.001*
Yoghurt (/day)	90.2 ± 106.6	101.8 ± 99.9	.07
Curd (g/day)	29.1 ± 46.3	33.3 ± 43.0	.25
Total dairy products (g/day)	339.0 ± 300.6	309.4 ± 238.7	.08
Lactose (g/day)	16.4 ± 14.8	14.9 ± 11.7	.07

Note. *Bold font indicates statistical significance.

Table 9. The Average Daily Consumption of Milk, Yoghurt, Curd, Total Dairy Products and Lactose in Males (g/day) (mean ± SD).

	CC	CT/TT	<i>p</i>
	(<i>n</i> = 90)	(<i>n</i> = 410)	
Milk (g/day)	174.6 ± 189.2	229.6 ± 252.6	.05*
Yoghurt (/day)	101.9 ± 105.8	87.7 ± 103.1	.24
Curd (g/day)	32.1 ± 50.5	28.4 ± 45.3	.49
Total dairy products (g/day)	308.6 ± 271.1	345.7 ± 306.6	.29
Lactose (g/day)	14.8 ± 13.1	16.8 ± 15.1	.26

Note. *Bold font indicates statistical significance.

association between LP allele and adiposity measures responds to a potential threshold effect of lactose consumption which was not achievable for girls in that sample (Larson et al., 2006).

We observed that the C/T-13910 LCT SNP presented a strong association with forearm circumference, in both groups of men; that is, those with BMI < 25 and with BMI > 25. Waist circumference was statistically connected with C/T-13910 LCT polymorphism only in the group of

men with BMI < 25. Anthropometrical measurements were higher in LNP men. Moreover, higher forearm circumference has been commonly associated with higher grip strength (Anakwe & Standley, 2006). In clinical trials, hand strength is used to predict the overall physical strength and health (including regression of muscle strength) (Bohannon, 2015). Importantly, hand grip strength could be impaired in obese people, due to their sedentary lifestyle and low physical fitness (Stenholm et al., 2011).

Table 10. The Average Daily Consumption of Milk, Yoghurt, Curd, Total Dairy Products and Lactose in Females (g/day) (mean \pm SD).

	CC	CT/TT	<i>p</i>
	(<i>n</i> = 137)	(<i>n</i> = 363)	
Milk (g/day)	158.1 \pm 179.1	181.8 \pm 181.6	.19
Yoghurt (/day)	90.3 \pm 85.7	106.2 \pm 104.5	.11
Curd (g/day)	29.1 \pm 46.3	32.3 \pm 43.0	.48
Total dairy products (g/day)	278.4 \pm 221.4	321.1 \pm 244.1	.07
Lactose (g/day)	13.4 \pm 10.9	15.5 \pm 11.9	.08

Table 11. The Average Weekly Consumption of Milk, Yoghurt, Curd, Total Dairy Products and Lactose in Caucasian Population (g/week) (mean \pm SD).

	Male	Female	<i>p</i>
	(<i>n</i> = 500)	(<i>n</i> = 500)	
Milk (g/week)	1538.0 \pm 1701.9	1226.8 \pm 1267.4	.001*
Yoghurt (g/week)	631.5 \pm 725.2	712.8 \pm 699.1	.07
Curd (g/week)	203.4 \pm 323.9	226.0 \pm 301.0	.25
Total dairy products (g/week)	2372.9 \pm 2104.2	2165.7 \pm 1670.7	.08
Lactose (g/week)	115.0 \pm 103.2	104.2 \pm 81.9	.07

Note. *Bold font indicates statistical significance.

Table 12. The Average Weekly Consumption of Milk, Yoghurt, Curd, Total Dairy Products and Lactose in Males (g/week) (mean \pm SD).

	CC	CT/TT	<i>p</i>
	(<i>n</i> = 90)	(<i>n</i> = 410)	
Milk (g/week)	1221.6 \pm 1324.5	1607.5 \pm 1767.9	.001*
Yoghurt (g/week)	713.3 \pm 740.8	613.5 \pm 721.4	.07
Curd (g/week)	225.0 \pm 353.8	198.6 \pm 317.2	.48
Total dairy products (g/week)	2159.9 \pm 1897.8	2419.6 \pm 2146.2	.29
Lactose (g/week)	103.9 \pm 91.5	117.4 \pm 105.7	.26

Note. *Bold font indicates statistical significance.

Table 13. The Average Weekly Consumption of Milk, Yoghurt, Curd, Total Dairy Products and Lactose in Females (g/week) (mean \pm SD).

	CC	CT/TT	<i>p</i>
	(<i>n</i> = 137)	(<i>n</i> = 363)	
Milk (g/week)	1106.4 \pm 1253.7	1272.3 \pm 1271.2	.02*
Yoghurt (g/week)	631.8 \pm 600.1	743.4 \pm 731.4	.11
Curd (g/week)	210.4 \pm 287.0	232.0 \pm 306.4	.47
Total dairy products (g/week)	1948.5 \pm 1550.1	2247.6 \pm 1708.9	.07
Lactose (g/week)	93.6 \pm 76.5	108.2 \pm 83.6	.08

Note.*Bold font indicates statistical significance.

Although the forearm circumference is an anthropological measurement used for calculating body components, its association with the C/T-13910 LCT

polymorphism has not been described yet. This may be due to the fact that such research among healthy and young individuals aged 18–38 has not been conducted to

Table 14. Association Between Polymorphism in Males and Females and Average Weekly Consumption of Milk, Yoghurt, Curd, Total Dairy Products and Lactose (g/week) (mean \pm SD).

	CC			CT/TT		
	Male (n = 90)	Female (n = 137)	p	Male (n = 410)	Female (n = 363)	p
Milk (g/week)	1221.6 \pm 1324.5	1106.4 \pm 1253.7	.51	1607.5 \pm 1767.9	1272.3 \pm 1271.2	.003*
Yoghurt (g/week)	713.3 \pm 740.8	631.8 \pm 600.1	.36	613.5 \pm 721.4	743.4 \pm 731.4	.01*
Curd (g/week)	225.0 \pm 353.8	210.4 \pm 287.0	.73	198.6 \pm 317.2	232.0 \pm 306.4	.14
Total dairy products (g/week)	2159.9 \pm 1897.8	1948.5 \pm 1550.1	.36	2419.6 \pm 2146.2	2247.6 \pm 1708.9	.22
Lactose (g/week)	103.9 \pm 91.5	93.6 \pm 76.5	.36	117.4 \pm 105.7	108.2 \pm 83.6	.18

Note. *Bold font indicates statistical significance.

date. Therefore, the association of the forearm circumference with C/T-13910 LCT polymorphism should be further investigated.

Another interesting finding of this study is the observation that LNP-carrier men have higher lean muscle mass, in comparison to LP (Table 4a). These observations are in line with other results obtained among Mediterranean population, in which the CC genotype was associated with lower BMI, lower waist circumference, and lower risk of obesity than the T allele even after adjusting for sex, age, diabetes, physical activity, and total energy intake (Corella et al., 2011). However, these authors did not analyze the association between the LCT polymorphisms and lean body mass in LNP individuals.

This result has implications for understanding the relationship between LCT and body composition, especially considering that the population variation in body composition has been linked to contemporary disease susceptibility (Gysel et al., 2014; Wells & Shirley, 2016).

Our previous report, on a smaller group of females ($n = 250$) (Popadowska & Kempinska-Podhorodecka, 2012), showed no relationship between the C/T-13910 LCT polymorphism and obesity, and this observation was confirmed in a large group of females (this study $n = 500$). Moreover, this study showed that higher milk and dairy products intake effected on increased fat mass in LP-carrier men. These results are in agreement with previous studies which confirmed a causal effect of higher dairy intake on increased BMI among adults (2018).

Some studies have confirmed a positive association between the LP allele and BMI (Almon et al., 2011; Corella et al., 2011; Kettunen et al., 2010). It can be explained by differences between LNP and LP, in terms of gut microbiota which may influence the caloric extraction of ingested food (Armougom et al., 2009; Suchy et al., 2010) or hormonal/peptide/fatty-acid constituents in milk having biological effects on consumers, which may potentially exert an effect on body composition (Adebamowo et al., 2008; Berkey et al., 2005). Furthermore, research conducted among children has

shown that the correspondence between LP and BMI was not statistically significant in this group (Almon et al., 2010). It is also worth mentioning that a negative association between dairy intake, regardless of fat content and BMI (Slyper & Huang, 2009), has been described, further implicating dairy products as both pro- and anti-obesogenic (Berkey et al., 2005; Lehtimaki et al., 2006; Remesar et al., 1999; Skinner et al., 2003). This is why, in order to understand the complex relationships among lactose intake (rather than dairy alone), genetic variation, and body composition, population-based research needs to be carried out; our research presented here comprises one such study.

It is worth to mention Smith's results, who observed that anthropometric, vascular, metabolic traits, socio-economic position, lifestyle, and fertility characteristics were largely unrelated to genotype. In Mediterranean women was dairy intake significantly lower in CC subjects (Corella et al., 2011). Apart from that, women who were homozygous for the C allele reported a higher prevalence of their general health being poor or fair, as compared to all other women (CT or TT), (Smith et al., 2009). In the same research, it was also observed that women who carried either one or two lactase non-persistence (C) alleles had higher HDLc than those who were homozygous for the T allele. Moreover, from research conducted in the 1990s, it appears that milk fat has been identified as cholesterol-elevating fat, as it contains cholesterol and is primarily saturated (Mistry & Hassan, 1991). Therefore, milk and high-fat dairy products contribute considerably to dietary fat milk intake and high-fat dairy products contribute considerably to dietary fat intake (Heaney, 2000). In our research, a lack of statistically significant results in the context of anthropometric measurements among women may be explained by their better care of appearance, which led to the statistically significant lower BMI among them, compared to that among men. The investigated women donated blood systematically and were better educated than the men, which may have led to pro-health eating habits.

Table 15. Association Between Polymorphism in Males and Females and Average Daily Consumption of Milk, Yoghurt, Curd, Total Dairy Products and Lactose (g/day) (mean \pm SD).

	CC			CT/TT		
	Male (n = 90)	Female (n = 137)	p	Male (n = 410)	Female (n = 363)	p
Milk (g/day)	174.6 \pm 189.2	158.1 \pm 179.1	.51	229.6 \pm 252.6	181.8 \pm 181.6	.003*
Yoghurt (g/day)	101.9 \pm 105.8	90.3 \pm 85.7	.36	87.7 \pm 103.1	106.2 \pm 104.5	.01*
Curd (g/day)	32.1 \pm 50.5	29.1 \pm 46.3	.73	28.4 \pm 45.3	32.3 \pm 43.0	.14
Total dairy products (g/day)	308.6 \pm 271.1	278.4 \pm 221.4	.36	345.7 \pm 306.6	321.1 \pm 244.1	.22
Lactose (g/day)	14.8 \pm 13.1	13.4 \pm 10.9	.36	16.8 \pm 15.1	15.5 \pm 11.9	.18

Note. *Bold font indicates statistical significance.

Table 16. Result of Simple Linear Regression Analysis and Pearson's Correlation Coefficients of Anthropometric Variables with Dairy Intake Among LP Men.

Anthropometric variables	Milk (g/week)		Yoghurt (g/week)		Curd (g/week)		Total dairy products (g/week)		Lactose (g/week)	
	r	p	r	p	r	p	r	p	r	p
Height (m)	.17	.12	.08	.45	.02	.82	.15	.15	.16	.14
Weight (kg)	.28	.01	.18	.09	.09	.38	.28	.01	.29	.01
Body mass index (kg/m ²)	.22	.04	.17	.11	.09	.43	.23	.03	.23	.03
Waist circumference (cm)	.22	.04	.21	.05	.09	.41	.25	.02	.25	.02
Hip circumference (cm)	.23	.02	.22	.04	.09	.38	.26	.01	.27	.01
Chest circumference (cm)	.19	.07	.25	.02	.13	.23	.26	.01	.26	.01
Forearm circumference (cm)	.04	.68	.23	.03	-.0004	.99	.12	.26	.13	.24
Shin circumference (cm)	.14	.18	.05	.67	-.03	.77	.08	.47	.08	.45
Fat mass (kg)	.30	.003	.16	.11	.11	.30	.30	.004	.30	.004
Lean mass (kg)	.20	.06	.17	.11	.05	.63	.22	.04	.22	.04

Note. r, Pearson's correlation coefficient; p < .05.

The men investigated in our study consumed significantly more lactose, compared with the women. Furthermore, a higher intake of milk and lactose was substantially connected with higher BMI among all investigated individuals (Table 7). One reason for this could be that there are differences between female and male sensitivities to the gastrointestinal symptoms caused by lactose, which are stronger in women (Remesar et al., 1999). Another reason could be that low lactose intake does not pose a problem, even for LNP. After such an intake of lactose, the gastrointestinal symptoms are not so troublesome unless >12g of lactose/day is consumed (Skinner et al., 2003). Other authors have emphasized that individuals who have problems with lactose digestion can tolerate foods containing less than 6 g lactose; that is, not more than 120 ml of milk (Slyper & Huang, 2009).

In Poland (according to IERiGI-PIB), in 2011, the average milk intake for one inhabitant was 193 liters (without considering milk used for production of butter). Considering its unique compounds (high content of calcium, phosphorus, potassium, magnesium, lead, manganese, cobalt, and B

vitamins—mainly riboflavin/vitamin B2) and favorable dietary properties, caterers all over the world have recommended the consumption of milk and dairy products daily. On the other hand, opponents have claimed that milk contains too much protein, too little phosphorus, low levels of assimilable calcium and, subsequently, can cause osteoporosis as dietary protein increases the production of acid in blood, which is then neutralized by calcium mobilized from the skeleton (Mattar et al., 2012). This theory has been confirmed by reports proving that countries such as the United States, England, and Sweden, which consume more milk, have higher rates of osteoporosis than China and Japan, where people eat much less protein and dairy food. Furthermore, calcium intake has demonstrated no protection in preventing bone fractures. In fact, those populations with the highest calcium intake have been shown to have higher fracture rates than those with more modest calcium intake (Abelow et al., 1992). Calcium balance is important in bone metabolism. Genetics, diet, and lifestyle factors influence the loss of bone integrity among many postmenopausal white women. According to research, the use

of animal proteins, salt, caffeine, and tobacco, as well as physical inactivity, cause calcium losses (Curtis et al., 2015).

Our study does have some limitations. Firstly, the study would benefit and perhaps findings would be strengthened if sample size, in particular with regards to lean males would be bigger. Moreover, we did not use a method such as bioelectrical impedance analysis (BIA), which produces consistent results and is commonly used to establish population norms. Our study relied heavily on indirect methods such as anthropometry, circumferences, or a combination thereof. Finally, further studies are needed to confirm our findings.

Conclusions

We found a significant dominance of the CC genotypes among women, compared with men. We reported the association between the C/T-13910 LCT polymorphism and body composition measures in Polish population. In our cross-sectional study it is hard to claim a causal inference nonetheless we suggest that in our cohort of Caucasian men the observed lactase persistence may be associated with higher dairy consumption and higher fat body mass, whereas lactase non-persistence may be related to reduced dairy consumption, and higher forearm circumference and lean body muscle mass. Further studies are required to confirm these findings. Genetic variation in the LCT gene may be important for understanding the relationship between the consumption of dairy products and nutrition status, as well as may lead to potential applications in human nutrition.

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